

CONTRACT PROGRESS REPORT

TITLE OF STUDY:	Community Studies on Pesticides
CONTRACT NO.:	PH 86-65-87
QUARTERLY PROGRESS REPORT NO.:	13
TIME PERIOD INVOLVED:	February 16 - May 15, 1968
DATE SUBMITTED:	June 7, 1968
PRIMARY CONTRACTOR:	California State Department of Public Health
PROJECT DIRECTOR:	Thomas H. Milby, M.D.
PRINCIPAL INVESTIGATOR:	Dudley Porter Miller, Ph.D.

CREDIT LINE AND DISCLAIMER

This is not a final report. Conclusions are subject to change on the basis of additional information and evidence. Information contained herein is not to be reprinted or published without written permission of the Office of Pesticides, Bureau of State Services (EH), Public Health Service, Washington, D.C. The views expressed herein are those of the investigators and do not necessarily reflect official viewpoint of the Public Health Service. This contract project is supported by the Office of Pesticides, Bureau of State Services (EH), Public Health Service, Washington, D. C.

COMMUNITY STUDIES ON PESTICIDES

Quarterly Progress Report #13
February 16 - May 15, 1968

California State Department of Public Health
Bureau of Occupational Health

TABLE OF CONTENTS

	<u>Page</u>
Abstract of this Report	1
Community Profile	2
Human Exposure to Lindane	4
Neonatal Jaundice Study in Imperial County	11
Long-Term Population Study	18
Pesticide Residues in Human Tissues	19
Investigation of Spills of Pesticides on Highways	21

ABSTRACT

This report presents progress made during the period February 16 - May 15, 1968 on the project's work units concerned with Community Profile, Neonatal Jaundice, Pesticide Residues in Human Tissues, and the Long-Term Study of Selected Populations Occupationally Exposed to Pesticides.

An article, prepared for publication and submitted to the National Communicable Disease Center for approval, is synoptically presented.

Several incidents involving spillage of pesticides on California highways are described and their management discussed.

Due to the continuing unavailability of Birth and Fetal Death Certificates, no progress on the study of Birth Defects and the possible causal relationship of Captan can be reported.

No fatal agricultural aircraft crashes have been reported either during the period of this report or during the first five months of the current calendar year.

No acute poisonings from pesticides have been reported during the period of this report.

COMMUNITY PROFILE

This study involves gathering descriptive information on pesticide usage, meteorological data, mortality and morbidity rates, economic characteristics, educational achievement, demographic characteristics and environmental monitoring in Imperial County, California. The completed Community Profile will be submitted at the end of 1968 as part of our annual report.

During the period of this report, acquisition of Community Profile data has centered in the two areas of environmental monitoring and demographic characteristics.

Environmental Monitoring

Due to the requirements of other work units, laboratory time to analyze environmental samples (i.e., food, water, air) for pesticide content is limited. Consequently, the aid of other agencies has been elicited to secure this information.

The Federal Food and Drug Administration operates its own laboratories for testing foods and has agreed to do one "Market Basket" or "Total Diet" Survey in Imperial County (probably in September, 1968) and to make available the results of their pesticide analyses. The foods will be selected from retail stores and will include the items in the diet of a typical 17 to 19 year old male over a two-week period.

Demographic Data

All of the demographic material to be included in the Community Profile has been collected.

On February 2, 1966, the Bureau of the Census, to meet its responsibilities under the Voting Rights Act of 1965, concluded a special census for Imperial County. The special census report contains the characteristics of the population by age, sex and race and its increase over the 1960 census figures. Population data for the Community Profile report will be based on these figures.

In June of 1966, the Department of Commerce informed the County Supervisors that Imperial County statistically qualified under the Public Works and Economic Development Act of 1965 for designation as a redevelopment area provided the County submitted an acceptable Overall Economic Development Plan by January 1, 1967. The OEDP, prepared by a committee of civic and business leaders, is the mainstay of the demographic section in the Community Profile, since it used statistics from the 1960 census and combined these with a detailed description of Imperial County's industry, agriculture, schools, public services and population.

Information to be included in the Community Profile from the 1960 census includes the growth of non-metropolitan areas of California from 1910 to 1960 and compares the growth of Imperial County with other non-metropolitan areas in California. Also included in the report will be selected characteristics of the Imperial County population such as marital status, projected

County future population, household relationships, mother tongue of the foreign born population, country of origin of the foreign stock, median school years completed, number and distribution of employed persons by occupation and industry and elements of personal income.

The latest figures (1965 to 1967) on the average civilian labor force, employment and unemployment are available from the California Department of Employment and will be included.

The Professional and Vocational Board for the State of California publishes a listing of licensees in the State by county. The Community Profile will compare the number of licensees in certain occupations with Statewide totals for the same occupations. Also, a distribution of Imperial County physicians, in total number, by selected specialties, and in private practice and hospitals has been obtained from the American Medical Association and will become part of the report.

During the next quarter, work plans for this unit include a report of the County's agriculture, which predominates its economic activities; organizing the accumulated morbidity and mortality data and a study of the County's water distribution and discharge systems.

HUMAN EXPOSURE TO LINDANE

Blood Lindane Levels as a Function of Exposure

Seventy-nine individuals exposed to the chlorinated hydrocarbon pesticide, lindane, were studied. Primary attention was focussed on blood lindane content as a function of intensity and duration of exposure.

Seventy-one individuals worked in lindane processing plants. Eight subjects received no occupational exposure but resided in households in which lindane vaporizers were operated intensively.

Results indicate that, in the individual, blood lindane content is a reflection of recent lindane absorption. Among groups exposed regularly to lindane, mean blood lindane levels appear to be a valid indicator of relative exposure intensities. Blood lindane levels do not appear to increase with increasing duration of exposure.

* * * * *

INTRODUCTION

Lindane is the gamma isomer of the chlorinated hydrocarbon pesticide benzene hexachloride (hexachlorocyclohexane, $C_6H_6Cl_6$). Like most other members of the family of pesticides loosely referred to as chlorinated hydrocarbons, lindane 1) exerts its principal acute toxic effect on the central nervous system, 2) is capable of producing liver and kidney changes in some experimental animals, and 3) may be stored in small quantities in the body fat without apparent effect.

During the past 15 years, a number of reports have been published in this country and elsewhere which suggest that lindane is capable of causing serious blood dyscrasias, primarily aplastic anemia(1,2,3). Since it has been repeatedly demonstrated that a variety of drugs and chemicals may cause bone marrow damage, these reports have been the subject of considerable interest among physicians as well as manufacturers and users of lindane. In her recent review of the problem, West(4) has described some aspects of the regulatory action which has been stimulated by governmental reaction to this situation.

Review of the several case reports which associate lindane and aplastic anemia reveals a common characteristic: each describes one or more patients who 1) suffer from erythropoietic depression, and 2) have had recent or, in some instances, remote exposure to lindane. While in most cases the hematological diagnosis is supported by convincing evidence, exposure relationships are sometimes less well documented. This is especially bothersome where other chemicals, often other pesticides, are involved along with lindane.

Since blood dyscrasias are not uncommon and the use of lindane is quite widespread, the opportunity for a chance rather than a causal association must be carefully considered. Unfortunately, as of this writing, there is no safe

clinical, serological, or biochemical method to determine, with certainty, whether a suspected drug or chemical is involved causally in the individual case of marrow failure. Moreover, very little is known about the dynamics of lindane absorption and elimination in man. In view of these uncertainties, we undertook a study of three groups of individuals exposed to lindane; one group at home and two groups at work. We sought first to determine the relationship between blood lindane content and lindane exposure, both recent and long term. We then carried out a series of clinical and biochemical studies to determine whether there existed among our populations any evidence of health impairment which could be related to lindane exposure. These studies stressed, but were not limited to, an assessment of hematopoiesis.

This report will be limited to a discussion of blood lindane levels as a function of lindane exposure. The clinical and biochemical aspects of exposure to lindane will be considered in a subsequent publication.

METHODS

Study Population

The study population consisted of 79 individuals, all of whom had been exposed to lindane on a daily basis for periods varying from a few weeks to many years. Seventy-one of these individuals were employed in 2 plants in which processing of lindane constituted the major activity. No other pesticides were processed in either of these plants. The remaining eight had no occupational exposure to lindane but comprised the residents of two households in which lindane vaporizing devices were operated for pest control purposes.

Each participant was interviewed with special reference to past and present illnesses, use of drugs, home exposure to chemicals, and home use of lindane vaporizing devices. In addition, a detailed occupational history was recorded. A specimen of venous blood was obtained from each subject and analyzed for lindane content using the hexane extraction method recently reported by Dale, et al⁽⁵⁾.

Environmental Appraisal

Multiple air samples were collected at each of the 2 lindane processing plants and in the 2 homes in which the 8 non-occupationally-exposed study subjects resided.

Samples were collected after the method of Miles, et al⁽⁶⁾, with the following modifications: air, metered through a glass frit bubbler at the rate of 500 cc/min., was passed through 20 ml of ethylene glycol. The collecting container consisted of a midget impinger with the glass frit bubbler replacing the impinger shaft. Suction was provided by a battery-operated MSA Monitaire pump. The sampling period was 15 minutes. In the laboratory, the glycol was extracted with pesticide-grade hexane and analyzed for lindane by electron capture gas chromatography.

Assessment of skin contact with lindane was made by observation of work practices among the employees in both plants. In addition, special attention was given to possible exposures to other toxic chemicals.

RESULTS

Lindane Exposure

An estimate of intensity of lindane exposure was formulated based on observations of work practices, knowledge of lindane sources, and actual air sampling. The study population was divided into 5 groups in accordance with these estimates. These groups, in order of increasing exposure are:

Group A

Twenty-one adults, employed in the 2 study plants, who worked in offices or shops and neither had direct contact with lindane nor worked in areas where lindane was processed.

Group B

Seven children and one adult who lived in homes in which lindane vaporizing devices were installed. Two households were represented. In each, 3 vaporizing devices had been operated on a daily basis for more than ten years.

Group C

Four production workers in one of the study plants who worked directly with lindane. They appeared to have little or no skin contact with lindane, which was processed in a granular form.

Group D

Thirty-two production workers in a second study plant who worked in a large room where lindane-containing products were processed and stored, but who did not regularly come into skin contact with these products.

Group E

Thirteen production workers in the second study plant who worked directly with lindane-containing products or who repaired and maintained lindane-processing machinery. Skin contact with lindane-containing products or lindane-contaminated equipment appeared to be frequent and prolonged.

Blood Lindane Levels

Mean blood lindane levels among the 5 groups studied are summarized in Table I. Mean values from 28 non-exposed controls are included for comparison. Results of air samples collected at the time blood specimens were obtained are also shown.

From this Table it is evident that mean blood lindane levels increase in a rather orderly manner according to estimated exposure intensity. The importance of skin contact is evident in Group E.

The Table also points out that air concentrations of lindane generated by home vaporizing devices can exceed air levels found in lindane processing plants.

In order to examine the effect of exposure time on blood lindane content, mean blood lindane values were calculated by years employed. Group D was chosen for this comparison because of its relatively large size and even distribution of exposure years. Table II shows this comparison and suggests that blood lindane content does not increase significantly with years of exposure.

DISCUSSION

Others have reported that lindane can be absorbed through the gastrointestinal tract, the respiratory tract, and the intact skin⁽⁷⁾. Little is known, however, of the quantitative relationships in man between intensity of skin or respiratory exposure to lindane and blood lindane content. We have shown that the blood of individuals with no occupational or home vaporizer exposure to lindane contains little or no detectable lindane. Among those with known exposure, blood lindane levels increase as air and skin exposure become more intense, but not as duration of exposure increases. These findings suggest that in man, blood lindane content is primarily a reflection of recent lindane absorption. Moreover, in groups of individuals exposed to lindane on a regular basis, mean blood lindane content appears to be a valid indication of relative exposure intensity.

TABLE I

Blood Lindane Content and Air Lindane Concentrations
By Exposure Group

	Lindane in Whole Blood (PPB)*			Lindane in Air Micrograms/m ³	
	No. Samples	Mean	Range	No. Samples	Range
<u>Controls</u> - No occupational or home vaporizer exposure	4 24	0.3** 0.46	- 0.3-0.9	- -	- -
<u>Exposed Group</u>					
A. Non-production workers in office and shops of plants using lindane	21	0.93	0.3-2.5	9	9.0-49
B. Lindane exposure from home vaporizer only (includes 7 children)	8	2.2	0.9-5.2	24	1.0-110
C. Production workers in lindane plant I (little or no skin contact)	4	4.6	1.9-8.3	12	31-1800
D. Production workers in lindane plant II (little or no skin contact)	33	4.1	1.0-8.9	14	11-1170
E. Production workers in lindane plant II (ample skin contact)	13	30.6	6.0-93.0	14	11-1170

*Parts per billion

**0.3 PPB is smallest amount detectable by the method used

TABLE II

Mean Blood Lindane Levels Among Individuals in Group D
By Years Employed

Years Employed	No.	PPB* Lindane	
		Mean	Range
<1	10	3.2	1.8-6.7
1-4	6	4.5	3.6-6.7
5-9	6	4.0	3.1-6.3
10-14	5	4.4	1.0-7.9
15+	6	5.1	2.7-8.9
All Years	33	4.24	1.0-8.9

* PPB = Parts per billion.

REFERENCES

1. Best, W.R.: Drug-Associated Blood Dyscrasias. J. Am. Med. Assoc. 185:286, 1963.
2. Sánchez-Medal, L.; Castanedo, J.P.; and García-Rojas, F.: Insecticides and Aplastic Anemia. New Eng. J. Med. 269:1365, 1963.
3. Loge, J.P.: Aplastic Anemia Following Exposure to Benzene Hexachloride (Lindane). J. Am. Med. Assoc. 193:110, 1965.
4. West, I.: Lindane and Hematologic Reactions. Arch. Environ. Health, 15:97, 1967.
5. Dale, W.E.; Curley, A.; and Cueto, C., Jr.: Hexane Extractable Chlorinated Insecticides in Human Blood. Life. Sci. 5:47, 1966.
6. Miles, J.W.; Fetzler, L.; and Pearce, G.W.: Collection and Determination of Trace Quantities of Pesticides in Air. Presented at the 149th Meeting of the American Chemical Society, 1965.
7. A.M.A. Council on Pharmacy and Chemistry. Committee on Pesticides. Toxic Effects of Technical Benzene Hexachloride and Its Principal Isomers. J. Am. Med. Assoc. 147:571, 1951.

NEONATAL JAUNDICE STUDY IN IMPERIAL COUNTY

In Quarterly Report No. 12, the data collection processes were described. At the time, there was an effective backlog of four weeks of uncollected data on mothers and their newborns. Since then, the backlog has been reduced by one week. It had been expected that the staff would catch up this quarter but an unusually large March birth rate, the development of the preliminary statistics presented in this report, and the collection of additional data took more staff time than had been anticipated. If the work load remains constant, the backlog will be absorbed during the ensuing quarter.

Two A.I.S.I., Model F-2-SER, Air and Gas Samplers, received from Research Appliance Company, were tested and put into operation March 21, 1968. These samplers incorporate a densitometer in the air sampling nozzle, and an automatic recorder which charts the change of light transmittance through the filter paper as air is drawn through it. The sampling rate being used is about 20 cubic feet per hour, and the sampling period is 3 hours. A sampler was placed on the roof of each of the two participating hospitals. The chart paper is removed from each recorder weekly for data collection. The average daily particulation for the six weeks preceding birth will be coded for all children born after May 1, 1968. Agricultural chemical usage and meteorological data are also being obtained as discussed in the last report.

In the four months since the collection of data began, 265 children have been born in the two hospitals taking part in the study. Hospital records and the mother's medical history have been obtained for all cases. No home interviews have been attempted for 25 of these children, either because no bilirubin test was made (9 cases) on the child, or because the family lives out of Imperial County (16 cases). In addition, 18 interviews from the latter part of March are pending. Thus, 222 of the possible 240 interviews have been attempted. Of these, 202 have been completed, 6 mothers have refused to be interviewed, and 14 families have moved from the County within 4 weeks after the birth of the child (See Table I).

The percentage of successful attempts to interview is 91.0%, surprisingly high in a population containing crop buyers, migratory workers and military personnel. Much of this success must be attributed to the cooperation of the local physicians who have explained the program to their patients, and to an article in the San Diego Union.

Selected statistics from the first four months of the program have been prepared by the resident staff. These statistics may be indicative of the final results of the study, as they represent one month (December, 1967) of historically high incidence of hyperbilirubinemia, and three months (January through March, 1968) of historically low incidence. This parallels the past yearly pattern of nine months (January through September) of low incidence and three months (October through December) of high incidence.

The mean bilirubin level for the four months is 7.03 mg%, with a standard deviation of 3.64 mg%. The median is 6.69 mg%, and the distribution is positively skewed. The mean bilirubin level for December is 8.1 mg%, for January 6.4 mg%, for February 7.0 mg%, and for March 6.6 mg% (See Table II).

If a case of hyperbilirubinemia is defined as a total bilirubin level of at least 10 mg%, the incidence for the first four months of the study was 20.3%. The incidence for December, however, was 32.8%, and for the following three months was less than 18%. The difference is statistically significant at the 99% confidence level (See Table III). If, however, the level of jaundice is defined as those values falling above one standard deviation from the mean (at least 10.7 mg%), the overall incidence drops to 15.6%. The incidence for December is 25%, and for January through March is 12.5%. The difference is statistically significant at the 98% confidence level (See Table IV).

When the study was established, it was agreed that the hospitals would try to take the bilirubin samples during the third day of life. Several factors, including the child's condition and the day of discharge, make absolute conformity impossible. Nonetheless, 184 of the 256 bilirubin samples were taken from the sixty-first through the eighty-fourth hour of life. Only 22 were taken later than the eighty-fourth hour.

Nine samples were taken during the second day of life (25 through 48 hours). The mean bilirubin level for the group is 5.86 mg%. During the third day of life (49 through 72 hours), 134 samples were taken. Their mean was 7.17 mg%. During the fourth day of life (73 through 96 hours), 104 samples were taken with a mean of 7.13 mg%. Nine samples, with a mean of 5.23 mg%, were taken later than the fourth day of life. The highest mean, 7.23 mg%, occurred in the group of 93 samples taken between the sixty-first and the seventy-second hour of life. Thus, the means for the third and fourth day of life are close enough so that these two days need not be given separate statistical analysis (See Table V).

Only 11.1% of the samples taken during the second day of life were above 10.6 mg% (one standard deviation from the mean); 14.9% of the samples taken on the third day, 16.3% of the samples taken on the fourth day, and 22.2% of the samples taken later than the fourth day were above this level. These differences are not statistically significant. The direction of increase is as would be expected, however.

Of the 256 children in the study, 145 were born at El Centro Community Hospital, and 111 at Pioneer's Memorial Hospital. The percentage of interviews completed is approximately the same for the two hospitals (See Table I).

The overall mean bilirubin level for children born at P.M.H. is 7.43 mg% with a standard deviation of 4.13; the mean for children born at E.C.C.H. is 6.73 mg% with a standard deviation of 3.20. The mean at P.M.H. is greater than the mean at E.C.C.H. for each of the four months under consideration, and the corresponding standard deviation is also greater for each month. These differences are not statistically significant above the 85% confidence level. They are, however, suggestive. Additional data are needed before it can be decided whether or not the data from the two hospitals can be treated statistically as one set of data (See Table II).

Only 11.0% of the bilirubin tests done at E.C.C.H. fall above 10.6 mg% (one standard deviation from the overall mean), but 21.6% of the P.M.H. tests fall above this level. This difference is significant at the 98% confidence level (See Table VI). When the data from the two hospitals are considered separately, bilirubin levels of at least 10.0 mg% for E.C.C.H. and bilirubin levels of at least 11.6 mg% for P.M.H. fall at least one standard deviation above the respective means. Then, 13.8% of the E.C.C.H. values fall above one standard deviation from the E.C.C.H. mean, and 16.2% of the P.M.H. values fall above one standard deviation from the P.M.H. mean. The difference between these values is not statistically significant. Other things remaining equal, this would tend to support separate treatment.

Since February 1, 1968, by arrangement with the project, hemoglobin and hematocrit tests have been done for every child born in E.C.C.H. Hemoglobin tests had not been done routinely before this time. They are frequently done at P.M.H. Of the 256 babies for which bilirubin tests were done, 198 of them also had hemoglobin tests. High hemoglobin level correlates with high bilirubin level. Of the 76 cases with hemoglobin levels of at least 20 gm%, 22 had bilirubin levels of at least 10 mg%. Only 19 of the 122 cases with hemoglobin levels under 20 gm% had bilirubin levels above 10 mg%. This difference is significant at the 95% confidence level (See Table VII).

The sex of the child does not correlate with the incidence of jaundice. A slightly larger proportion of the males than of the females (27 out of 124 compared with 25 out of 134) had bilirubin levels of at least 10.0 mg%, but this difference is not significant (See Table VIII).

The method of feeding does not correlate with the incidence of neonatal jaundice. Sixteen percent of the breast fed children were jaundiced compared with 23% of the bottle fed children, but this difference is not statistically significant (See Table IX).

Data will be available for additional analyses in which premature babies and those with high direct bilirubin levels will be eliminated. The present preliminary analysis has been done for two reasons: to suggest directions of fruitful analysis and to make available some preliminary results to those interested in the study.

SUMMARY

1. In the first four months of the study, follow-up will be complete for 90% of the children in it.
2. Mean bilirubin level for the first four months is 7.03 mg% with a standard deviation of 3.64 mg% in a positively skewed distribution.
3. Two definitions of hyperbilirubinemia are available:
 - a) total bilirubin $\geq$ 10.0 mg%;
 - b) total bilirubin $\geq$ one standard deviation from the mean, in this case $\geq$ 10.7 mg%.
4. The incidence of jaundice by definition (a) is 20.3%, and by definition (b) is 15.6%.
5. By either definition, the incidence in December is statistically greater than the incidence in the following three months.

6. Only 18 of the 256 cases may have to be considered separately because the tests were done too early or too late.
7. Maximum mean bilirubin level occurred for samples taken between two and a half and three days after birth.
8. Approximately 57% of the children were born at El Centro Community Hospital; the remaining 43% were born at Pioneer's Memorial Hospital.
9. The mean bilirubin level is lower, the standard deviation is smaller, and the incidence of neonatal jaundice is lower at El Centro Community Hospital, but not to a statistically significant level.
10. It is probable that these differences are a reflection of the fact that two different laboratories are involved, rather than that the populations differ.
11. It was expected that the data from the two hospitals would have to be treated statistically as distinct samples, as a control; this expectation appears valid.
12. There is a significantly higher incidence of neonatal jaundice among newborns with hemoglobin levels of at least 20 gm% than among newborns with lower hemoglobin levels.
13. There is no significant difference in the incidence of hyperbilirubinemia between the sexes, nor between the breast fed and the bottle fed babies.

TABLE I

Results of Follow-Up by Month of Birth, by Hospital

	Total Children Born	Bilirubins Not Done	In Study	Reside Out of County	Possible Interviews	Attempted Interviews	Pending	Complete Interviews	Uncompleted Interviews	
									Moved Out of County	Refused Interview
Total	265	9	256	16	240	222	18	202	14	6
Dec. '67	68	4	64	2	62	62	--	60	2	--
Jan. '68	60	1	59	6	53	53	--	47	4	2
Feb. '68	67	2	65	4	61	61	--	54	4	3
Mar. '68	70	2	68	4	64	46	18	41	4	1
PMH	116	5	111	5	106	89	17	81	5	3
ECCH	149	4	145	11	134	133	1	121	9	3

TABLE II

Number of Newborns, Mean Bilirubin Level, and Standard Deviation by Month of Birth

	Number of Newborns			Mean Bilirubin Level (mg%)			Standard Deviation (mg%)		
	Total	PMH	ECCH	Total	PMH	ECCH	Total	PMH	ECCH
Total	256	111	145	7.03	7.43	6.73	3.64	4.13	3.20
Dec. '67	64	32	32	8.12	8.76	7.49	4.36	4.90	3.72
Jan. '68	59	21	38	6.36	6.40	6.34	3.20	3.61	2.99
Feb. '68	65	28	37	6.99	7.29	6.76	3.63	4.51	3.08
Mar. '68	68	30	38	6.63	6.85	6.46	3.08	3.12	3.07

TABLE III (a)

Number Jaundiced (B/R ≥ 10 mg%)
By Month of Birth, with Percent of Total

	Total	Bilirubin ≥ 10 mg%	% of Total
Total	256	52	20.3
Dec. '67	64	21	32.8
Jan. '68	59	8	13.6
Feb. '68	65	11	16.9
Mar. '68	68	12	17.6

(a) $\chi^2 = 8.23$, $df = 1$, $p < 0.01$

TABLE IV (b)

Number Jaundiced (B/R ≥ 10.7 mg%)
By Month of Birth, with Percent of Total

	Total	Bilirubin ≥ 10.7 mg%	% of Total
Total	256	40	15.6
Dec. '67	64	16	25.0
Jan. '68	59	6	10.2
Feb. '68	65	10	15.4
Mar. '68	68	8	11.8

(b) $\chi^2 = 5.69$, $df = 1$, $p < 0.02$

TABLE V

Selected Bilirubin Statistics by Day of Life Bilirubin Taken

	Total	Mean Bilirubin mg%	Bilirubin ≥ 10.0 mg%	% of Total	Bilirubin ≥ 10.7 mg%	% of Total
Total	256	7.03	52	20.3	40	15.6
Taken 2nd Day	9	5.86	2	22.2	1	11.1
Taken 3rd Day	134	7.17	28	20.9	20	14.9
49-60 Hrs.	41	7.04	9	22.0	9	22.0
61-72 Hrs.	93	7.23	19	20.4	11	11.8
Taken 4th Day	104	7.13	20	19.2	17	16.3
73-84 Hrs.	91	6.93	15	16.5	12	13.2
85-96 Hrs.	13	8.56	5	38.5	5	38.5
Taken After 4th Day	9	5.23	2	22.2	2	22.2

TABLE VI(c)

Number Jaundiced (B/R ≥ 10.0 mg% and ≥ 10.7 mg%) by Hospital of Birth

	Total	Bilirubin ≥ 10.0 mg%	% of Total	Bilirubin ≥ 10.7 mg%	% of Total
Total	256	52	20.3	40	15.6
PMH	111	32	28.8	24	21.6
ECCH	145	20	13.8	16	11.0

(c) $\chi^2 = 5.42$, df = 1, $p < 0.02$

TABLE VII(d)

Bilirubin Level
by Hemoglobin Level

	Total	Bilirubin	
		< 10 mg%	≥ 10 mg%
Total	198	157	41
Hgb < 20	122	103	19
Hgb ≥ 20	76	54	22

(d) $\chi^2 = 5.17$, df = 1, $p < 0.05$

TABLE VIII

Bilirubin Level
By Sex

	Total	Bilirubin	
		< 10 mg%	≥ 10 mg%
Total	256	204	52
Male	124	97	27
Female	132	107	25

TABLE IX

Bilirubin Level
by Method of Feeding

	Total	Bilirubin	
		< 10 mg%	≥ 10 mg%
Total	256	204	52
Breast*	84	71	13
Bottle	172	133	39

* Includes those both breast and bottle fed.

LONG-TERM POPULATION STUDY

The objectives of this study and its planned procedure were presented in Quarterly Progress Report No. 12. Briefly, we have sought to establish a cooperative study population of individuals exposed to pesticides in the course of their occupations and to determine through a series of medical and biochemical tests the effect, if any, upon their health from exposure to pesticides over an extended period of time.

During the period of this report, baseline medical and biochemical information have been gathered from a group of 29 workers representing nine pest control firms in the San Jose area. These men were selected on the bases of an age range of 35 to 50 years, on their experience of five or more years of working with pesticides, and on their stated willingness to participate in the study over a period of five or more years.

The examination and tests performed upon these participants followed the plan described in Quarterly Progress Report No. 12, with two important additions. An electrocardiogram is performed on each worker, both with the man at rest and following a prescribed two-step exercise, and a pulmonary function determination is added in order to determine whether differences between individual hemoglobin levels can be correlated with differences in vital capacity.

Arrangements are being completed to conduct similar baseline medical and biochemical determinations upon a matched group of unexposed workers in the San Jose area who will serve as controls.

In examining other sources of appropriate, stable and cooperative populations of persons exposed to pesticides who might be included in the long-term study, attention has focussed on Agricultural Extension Specialists and County Farm Advisors who are affiliated with the University of California. Within the same organization is a large group of County 4-H Advisors who do not work with pesticides, and who, it is anticipated, will volunteer to participate in the study as control subjects.

During the period of this report, successful meetings have been held with the Director of the Agricultural Extension Service, University of California, and with several of his aides in order to explain the purpose and objectives of the study and to elicit their interest and support. The interest of the Extension Service in having its employees participate in the study has been established. Identification of approximately 50 workers who are interested in participating and who meet established criteria for entering the study is currently underway.

PESTICIDE RESIDUES IN HUMAN TISSUES

This activity is concerned with an accumulation of data on the levels of selected pesticides in human blood and fat collected at the time of autopsy in order to contribute to the total sum of knowledge on the body burden of pesticides among the general population. The study plan, in addition to obtaining and analyzing blood and fat specimens, includes securing individual death certificates to determine the cause of death, age, sex, race, last occupation and residence of the deceased for comparing and cataloging the group under study.

During the period of this report, with the cooperation of the Coroner's Office of Alameda County, the requested specimens were obtained from 105 autopsied former residents of the greater Oakland, California area together with matching death certificates.

The Pesticides Laboratory has completed hexane extractions on all 210 tissues and has completed its analyses for pesticides on 20 of the fat and 10 of the blood samples. This work has been temporarily suspended to permit the laboratory to concentrate on analyzing blood specimens from the long-term study population for pesticide levels and cholinesterase activity.

When the analyses of the entire 210 tissues is complete, the death certificate information and other information is gathered, including the deceased's occupational history and place of residence, each member of the study population will be assigned to a heavily-exposed group, to a minimally-exposed group, and to urban or rural-dwelling categories.

During this quarter, the results of the Pesticides Laboratory analyses of 36 tissues from the final 6 autopsies collected during contract year 1967 from Kern County were forwarded to the Office of Pesticides in Atlanta. These results are shown in the table. Upon completing laboratory analyses on a total of 232 tissues from 94 bodies autopsied, a retrospective study of the 80 among them who were residents of the County at the time of death was undertaken.

In cooperation with the Kern County Health Department and particularly its Public Health Nurses and Spanish-speaking Seasonal Farm Workers Health Aides, contact was made with next-of-kin, relatives, neighbors or previous employers of each of the deceased. Utilizing a questionnaire developed by project staff, the interviewers were able to secure sufficient information on exposure to pesticides for each of 71 of the deceased to be able to assign them to either a heavily-exposed or minimally-exposed group. Of the nine remaining cases, five on whom informants could not be located were persons employed for several years prior to death as "farm Laborers" and will be placed arbitrarily in the heavily-exposed group.

Presently, these data are now being correlated with laboratory analyses, Kern County Agricultural Commissioner's data on pesticide usage, and the Food and Drug Administration's "Market Basket" or "Total Diet" Survey data from Bakersfield. Upon completion of this work, a comprehensive written report will be sent to the Office of Pesticides.

Levels of Various Pesticides Found in Autopsy Tissue from Residents of

Kern County, California

Autopsy No.	Tissue	Percent Fat	Pesticides Found Indicated on a Fat Basis in p.p.m.						
			o,p' DDT	p,p' DDT	TDE	p,p' DDE	Dieldrin	B-BHC	Heptachlor Epoxide
C-264-67	Brain	8.7	-	0.14	-	0.5	-	-	-
	Gonad	3.7	-	0.57	-	1.5	-	-	-
	Liver	3.8	-	0.58	0.37	11	-	-	-
	Ventral Abdominal Fat	83	-	1.6	-	11	0.3	-	-
	Kidney	2.7	-	1.5	-	4.8	-	-	-
	Bone Marrow	30	-	0.95	-	5.7	-	-	-
C-281-67	Brain	9.5	-	0.21	-	0.65	-	-	-
	Gonad	2.1	-	1.4	-	4.0	-	-	-
	Liver	3.5	-	0.46	1.1	12	-	-	-
	Ventral Abdominal Fat	79	-	1.5	-	15	0.33	-	-
	Kidney	3.0	-	2.7	-	11	-	-	-
	Bone Marrow	24	-	2.3	-	10.8	-	-	-
C-317-67	Brain	10.5	-	0.12	-	0.40	-	-	-
	Gonad	3.9	-	0.74	-	2.1	-	-	-
	Liver	2.6	-	1.7	0.19	17	-	-	-
	Ventral Abdominal Fat	69	-	1.3	-	11	0.23	-	-
	Kidney	3.5	-	1.4	-	6.3	-	-	-
	Bone Marrow	22	-	1.0	-	5.7	-	-	-
C-318-67	Brain	11	-	0.22	-	0.89	-	-	-
	Gonad	3.4	-	2.1	-	7.8	-	-	-
	Liver	4.4	-	6.4	1.6	16	-	-	-
	Ventral Abdominal Fat	72	-	3.9	-	24	0.21	-	-
	Kidney	3.0	-	3.0	-	17	-	-	-
	Bone Marrow	33	-	2.6	-	22	-	-	-
C-329-67	Brain	10.3	-	0.20	-	0.41	-	-	-
	Gonad	3.1	-	0.61	-	1.7	-	-	-
	Liver	4.4	-	3.4	0.9	18	-	-	-
	Ventral Abdominal Fat	86	-	1	-	9	0.27	-	-
	Kidney	2.8	-	2.9	-	8	-	-	-
	Bone Marrow	37	-	1.4	-	5.4	-	-	-
C-335-67	Brain	10	-	0.17	-	0.66	-	-	-
	Gonad	3.9	-	0.52	-	2.0	-	-	-
	Liver	4.6	-	1.4	0.13	7	-	-	-
	Ventral Abdominal Fat	80	-	1.8	-	11	0.4	-	-
	Kidney	2.6	-	2.3	-	10	-	-	-
	Bone Marrow	27	-	1.4	-	7.1	-	-	-
C-336-67	Brain	9.7	-	0.50	-	0.99	-	-	-
	Gonad	2.0	-	0.16	-	7.3	-	-	-
	Liver	6.6	-	3.3	4.2	17	-	-	-
	Ventral Abdominal Fat	79	-	4.7	-	19	0.43	-	-
	Kidney	2.9	-	4.1	-	16	-	-	-
	Bone Marrow	19	-	6.3	-	22	-	-	-

INVESTIGATION OF SPILLS OF PESTICIDES ON HIGHWAYS

During the latter half of the period of this report, a rash of five incidents occurred involving spills of pesticides from trucks onto highways in the San Francisco Bay Area. Inasmuch as the circumstances of the spills were similar in each of the events, a description of but two of them is presented.

Event #I - April 17, 1968

At about 1:45 PM on April 17, 1968, the Agricultural Commissioner of a Bay Area County received a call from the District Office, California Division of Highways, that four ten-pound sacks of wettable powder containing a mixture of 12½% parathion and 18% malathion had apparently spilled from a truck onto the freeway in Castro Valley.

A landscape specialist, Division of Highways, working on the highway in the area at the time, discovered the ruptured sacks and, upon reading their labels, immediately recognized the hazard presented by the powder which was blowing about in a brisk wind. He arranged to have the sacks covered by canvas tarpaulins and the peripheral dust wetted down. The State Department of Agriculture in Sacramento was called and in turn called the decontamination team of a local pesticide manufacturer, whose products were not involved in the event. The team responded immediately and proceeded to decontaminate and remove the spilled pesticides. Lime and isopropyl alcohol were used liberally in the process following which the surrounding trees and hedges were washed down by the local fire department.

Residents living adjacent to the freeway were advised to wash down their houses and yards, to re-wash any laundry which had been on clotheslines at the time of the incident, and to keep pets and children out of the yards for the next 48 hours. All persons exposed to the spill were advised to shower, change to clean clothing and machine-wash all exposed clothing. In addition, all persons inadvertently exposed to the pesticides spilled were advised of the signs and symptoms of pesticide poisoning, to seek medical attention if they later became ill by notifying the police who had been given information about the pesticides and the antidotes for them. All of these activities were completed by 5:00 PM on the day of the incident. (Twenty-four hours after the spill, no illnesses had been reported).

Efforts to locate and identify the truck from which the spill occurred were unsuccessful over a period of several days but was eventually located. Lacking information about the truck, it was not possible to determine if it was engaged in interstate commerce and consequently under the jurisdiction of the Federal Department of Transportation, or was engaged in intrastate commerce and thus under the jurisdiction of the California Highway Patrol. Since parathion is a Class B Poison, after checking Title 49 of the Federal Code of Regulations, which has also been adopted by the California Highway Patrol, it appears that the incident may have revealed violations of one or more of the regulations concerned with the packaging, labelling, method of transport, or requirements on securing a load of pesticides while in transit.

The decontamination team visited the site again the next day to check the area and to collect soil and foliage specimens for delivery to the Department's

Pesticides Laboratory for analyses to determine whether any significant contamination at the site of the spill was persisting.

Subsequently, with the assistance of the chemical company which had manufactured the spilled pesticides, the truck engaged in transporting them was located in a town more than 200 miles distant from the spill. The conveyance consisted of a flat-bed truck and an attached trailer. At the point of origin, the load consisted of 900 bags of sulphur and "a few containers of the parathion-malathion pesticide were added to the load." The load was counted at the time of loading and again when it arrived at its destination which revealed no discrepancy in the count. Consequently, the trucker was unaware of the loss until the spill was investigated and the shipment traced. No investigation was made for contamination of the truck or trailer because of the lapse of time since the spill and the locating of the truck, and because it was assumed that the carton which contained the four sacks of pesticides had fallen from the truck and ruptured when it struck the pavement. Other information suggests, however, that the carton ruptured on the truck, spilling its contents onto the highway, especially since the container was found on the highway about one mile beyond the spill.

Event #11 - May 10, 1968

During the late evening of May 10, 1968, a District Superintendent of the California Division of Highways called the Department's Bureau of Occupational Health to advise that there had occurred at about 9:00 PM a spill on the Eastshore Freeway of 45% liquid parathion. Two 5-gallon drums of the chemical had fallen from a truck. A car following the truck had hit and ruptured one of the drums. The driver of the car stopped, picked up the drum and set it off the freeway. Other cars hit the second drum which was not ruptured. Subsequently, an estimated 300 cars drove through the area before the Highway Patrol could divert traffic around it. The three occupants of the car which struck and ruptured one of the drums, and six members of the Highway Patrol and their cars had been contaminated by the parathion concentrate. All were taken to a local hospital in Berkeley for observation and treatment.

The Highway Patrol was preparing to issue a bulletin designed to advise all persons who had ridden through the stretch of contaminated highway to seek medical attention. The toxicologist in the Bureau of Occupational Health advised the Highway Patrol to impress the fact that the incident involved a skin exposure problem and that persons who remained in closed automobiles would not be at risk since liquid parathion on a cool night out-of-doors would not be releasing significant amounts of toxic vapors. On the other hand, persons in contact with the spilled chemical through brushing against their cars or handling its wheels and tires which had been splashed by the chemical could become dangerously exposed and, therefore, decontamination of their vehicles was a most important step and should be so advised. The Highway Patrol bulletin was issued accordingly.

The physician in charge of poisoning cases at the local hospital was contacted by the Bureau of Occupational Health to alert him to the incident and to the probable early arrival of exposed persons for treatment. As it turned out, the three occupants of the private car and the six members of the Highway Patrol were just arriving at the hospital at the time the call was received. At the physician's request, the Bureau's toxicologists gave him information

about the incident, the chemical involved, the individuals involved, the character of their exposure and gave suggestions on their management. Similar information was given to the emergency service units at two additional area hospitals.

A decontamination team from a local pesticides manufacturing plant was called and immediately responded to the call as a public service since, as in Event #I, its products were not involved.

The truck from which the spill occurred, was a flat-bed conveyance loaded with 50 five-gallon drums of liquid parathion and pulling a flat-bed trailer loaded with dry pesticides.

The disaster squad at the local hospital was mobilized and took care of the nine exposed cases reporting to it in a manner which was exemplary and could serve as a model for other hospitals to follow in the treatment and management of pesticide poisoning cases. Each patient was undressed, showered, put to bed for overnight observation and blood drawn periodically for cholinesterase tests. None became ill. All washable clothing was properly bagged for automatic machine-washing. Boots, shoes and similar clothing were prepared for disposal as hazardous items. The ultimate management of these cases contrasted sharply with their management at the first hospital they reported to where they were told to wash their hands, then dismissed and advised to seek further medical attention if it became necessary.

From the two incidents discussed, from three similar and recent incidents, and from other incidents which occurred during the last five months, much concern has developed among officials of the State Departments of Public Health, Highways, Agriculture, Transportation and the California Highway Patrol and the Federal Transportation Agency over the transport of hazardous materials over California highways. Coupled with this concern is a growing awareness of a need for expert training of employees of these agencies in the management of incidents involving pesticides and of persons, equipment and environments exposed to them. Requests have been received by the Department's Bureau of Occupational Health from some of these agencies to undertake training sessions for their employees directed at these issues. The Motor Carrier Safety Section of the California Highway Patrol is proposing a new ruling wherein flat-bed trucks without rack sides could no longer be used to transport pesticides or other hazardous substances and wherein more rigorous security measures for trucks carrying Class B Poisons would be required. The Bureau is willing and anxious to be of all possible assistance in supporting constructive activities and proposals for more stringent controls in the transport, handling, storage, use, and safe management of pesticides and other hazardous substances.